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Prescribing decisions should be made based on the approved package insert in the country of prescription

Sponsor/company:	sanofi-aventis	**ClinicalTrials.gov Identifier:**	NCT00436800
		Study Code:	L_9281
Generic drug name:	Oxaliplatin	**Date:**	23 September 2009

Title of the study:	Study number: L9281 BILWEEKLY Gemcitabine and Oxaliplatin (GEMOX) in first-line metastatic or recurrent nasopharyngeal carcinoma (NPC) Short title: GEMOX-in-NPC	
Investigator(s):	Name : Prof Anthony TC CHAN, Dr. Brigette MA (Co-PI) Address : Department of Clinical Oncology, Prince of Wales Hospital, Shatin, Hong Kong Name : Dr. Tung Yuk Address : Department of Clinical Oncology, Tuen Mun Hospital, Tuen Mun, Hong Kong	
Study center(s):	2 centers (1) Prince of Wales Hospital, Hong Kong (2) Tuen Mun Hospital	
Publications (reference):	Annals of Oncology, 23 June 2009 [Epub ahead of print]	
Study period: Date first patient/subject enrolled: 21 Mar 2005 Date last patient/subject completed: 27 Oct 2008		Phase of development: Phase 2
Objectives:	Primary objective: • To evaluate the response rate of biweekly gemcitabine and oxaliplatin (the GEMOX regimen) in the first line treatment of metastatic or recurrent nasopharyngeal carcinoma (NPC) Secondary objective(s): • To assess the toxicity, duration of response, time to progression, progression-free survival, overall survival and cancer-related symptoms in the first line treatment of patients with metastatic or recurrent NPC	
Methodology:	single-arm, non-randomized, phase II trial	

Number of patients/subjects:	Planned: 40	Randomized: N/A	Treated: 41
Evaluated:	Efficacy/Pharmacodynamics: 40	Safety: 41	Pharmacokinetics: N/A
Diagnosis and criteria for inclusion:	○ Age above 18 years of age ○ ECOG PS 0-2 ○ Histologically or cytologically proven NPC with metastatic or recurrent disease that is not amenable to potentially curative surgery or radiotherapy (RT). They must not have prior chemotherapy for the treatment of metastatic or recurrent disease. ○ At least one uni-dimensional measurable lesion (according to RECIST criteria) ○ Prior RT or surgery to the target lesion(s) or prior neoadjuvant, adjuvant or concurrent chemotherapy is allowed as long as ≥ 6 weeks from last day of treatment. ○ Adequate hematological function: ● Absolute neutrophil count ≥ 1.5 x 109/L ● Platelet count ≥ 100 x 109/L ● Hemoglobin (Hb) ≥ 9 g/dL (patients may be transfused to achieve this requirement) ○ Adequate renal and hepatic functions: ● Serum creatinine ≤ 1.25 x (upper normal limit) UNL or a calculated creatinine clearance ≥ 50 mL/min ● Serum bilirubin < 2 x UNL ● AST/ALT ≤ 3 x UNL (≤ 5 x ULN if liver metastases present)		
Investigational product: Dose: Administration:	Oxaliplatin (+ Gemcitabine) Day 1: Gemcitabine at 1000mg/m2 administered as a 10mg/m2/min infusion, followed by Day 2: Oxaliplatin at 100mg/m2 over 2 hours The regimen is given every 2 weeks to a maximum of 12 cycles Oxaliplatin as 2-hours intravenous infusion Gemcitabine as a 100-min intravenous infusion		
Duration of treatment: The regimen is given every 2 weeks to a maximum of 12 cycles		Duration of observation: 1-year post treatment completion	
Reference therapy:	N/A		
Criteria for evaluation:			
Efficacy: Or Pharmacodynamics:	• Tumor response rate based on RECIST criteria • Duration of response • Time to progression • Progression-free survival • Overall survival • Cancer-related symptoms		
Safety:	Toxicity		
Pharmacokinetics:	N/A		

<table>
<tr><td>Pharmacokinetic sampling times and bioanalytical methods:</td><td>N/A</td></tr>
<tr><td>Statistical methods:</td><td>A null hypothesis of 35% versus an alternative hypothesis of 60% was tested. The reported range of responses for platinum-based doublets had been 38-70% (Yeo et al 1996, Yeo 1998, Au et al 1994, Ngan et al 2002). This estimated range also accounts for differences in patient population and response assessment criteria across different studies. A two-stage design by Simon (1989) will be used (Controlled Clin Trials, 10:1-10,1989). For a total of 39-40 subjects, 14 will be accrued during stage 1 and 25 during stage 2. Given that the 'true' response probability is 35%, there is a 64.05% probability of ending the trial during stage 1. However, if the 'true' response probability is 60% then there is a 5.83% probability that the trial will be stopped in stage 1. The alpha level of the design is 0.05 and the power is 0.9. If 5 or fewer responses are observed during the first stage then the trial is stopped early. If 18 or fewer responses are observed by the end of the trial then no further investigation of the drug is warranted. Given a 'bad' response rate of 35%, the expected sample size for the trial is 22.99. Summary: the target sample size will be 40 patients</td></tr>
<tr><td>Summary:</td><td>42 were recruited, of whom most (61%) had metastatic disease.

Of the 40 patients evaluated for response, the respective overall response and disease control rates were 56.1% and 90.2%.
At a median follow-up of 14.8 months, the respective median overall survival and time to progression were 19.6 months [95% confidence interval (CI) = 12.8–22 months] and 9 months (95% CI = 7.3–10 months). Grade 3–4 toxic effects were uncommon.</td></tr>
<tr><td>Efficacy results:
or
Pharmacodynamic results:</td><td><table>
<tr><td>Assessment</td><td>Results</td></tr>
<tr><td>Response rate (RR) based on RECIST criteria</td><td>Overall response = 56.1%

Disease control rates = 90.2%</td></tr>
<tr><td>Median overall survival</td><td>19.6 months [95% confidence interval (CI) = 12.8–22 months]</td></tr>
<tr><td>Median time to progression</td><td>9 months (95% CI = 7.3–10 months)</td></tr>
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<tr><td>Safety results:</td><td>Haematological toxicity:<table><tr><td>Hematological toxicity</td><td>G3-4
N (%)</td></tr><tr><td>Hemoglobin</td><td>1 (2%)</td></tr><tr><td>Lymphopenia</td><td>14 (34%)</td></tr><tr><td>Leucopenia</td><td>9 (22%)</td></tr><tr><td>Neutropenia</td><td>9 (22%)</td></tr><tr><td>Thrombocytopenia</td><td>7 (17%)</td></tr></table>Non-Haematological toxicity:<table><tr><td>Non-Hematological toxicity</td><td>G3-4
N (%)</td></tr><tr><td>Fatigue</td><td>20 (49%)</td></tr><tr><td>Sensory neuropathy</td><td>18 (44%)</td></tr><tr><td>Nausea</td><td>14 (34%)</td></tr><tr><td>Alanine transferase</td><td>8 (20%)</td></tr><tr><td>Diarrhoea</td><td>3 (7%)</td></tr><tr><td>Rash</td><td>1 (2%)</td></tr><tr><td>Hyponatremia</td><td>1 (2%)</td></tr><tr><td>Epistaxis</td><td>3 (7%)</td></tr><tr><td>Fever</td><td>4 (10%)</td></tr></table></td></tr>
<tr><td>Pharmacokinetic results:</td><td>N/A</td></tr>
<tr><td>Date of report:</td><td>14 Sept 2009</td></tr>
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